What was Old is New Again- the Use of Whole Blood for Civilian Trauma Resuscitation

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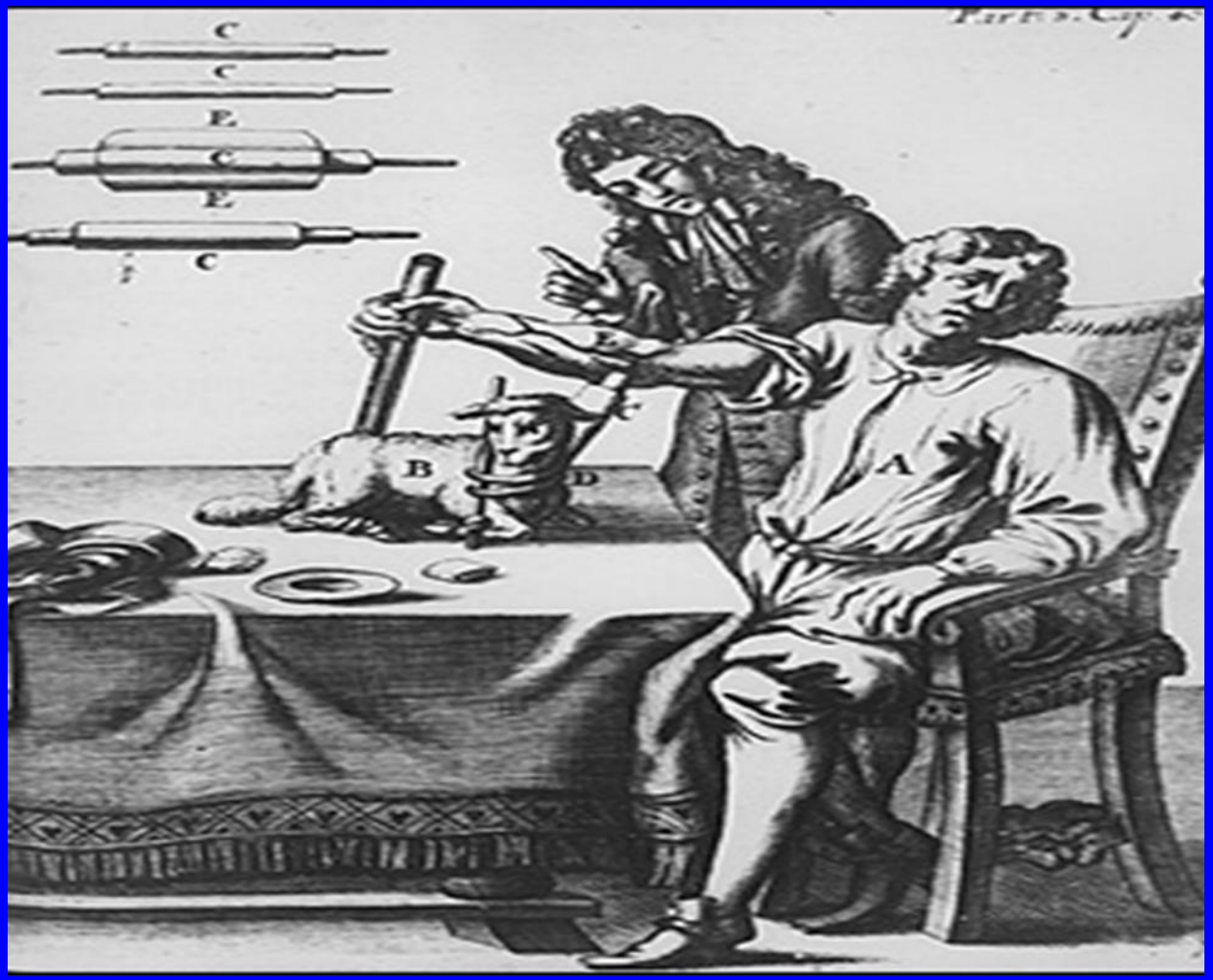
Disclosures

- Grífols: Honoraria & SAB
- Macopharma: Scientific advisory board
- Octapharma: Scientific advisory board
- Terumo: Honoraria
- Haemonetics: Honoraria
- Cook Biotech: Scientific advisory board
- Verax Biomedical: Scientific advisory board
- New Health Sciences: Scientific advisory board

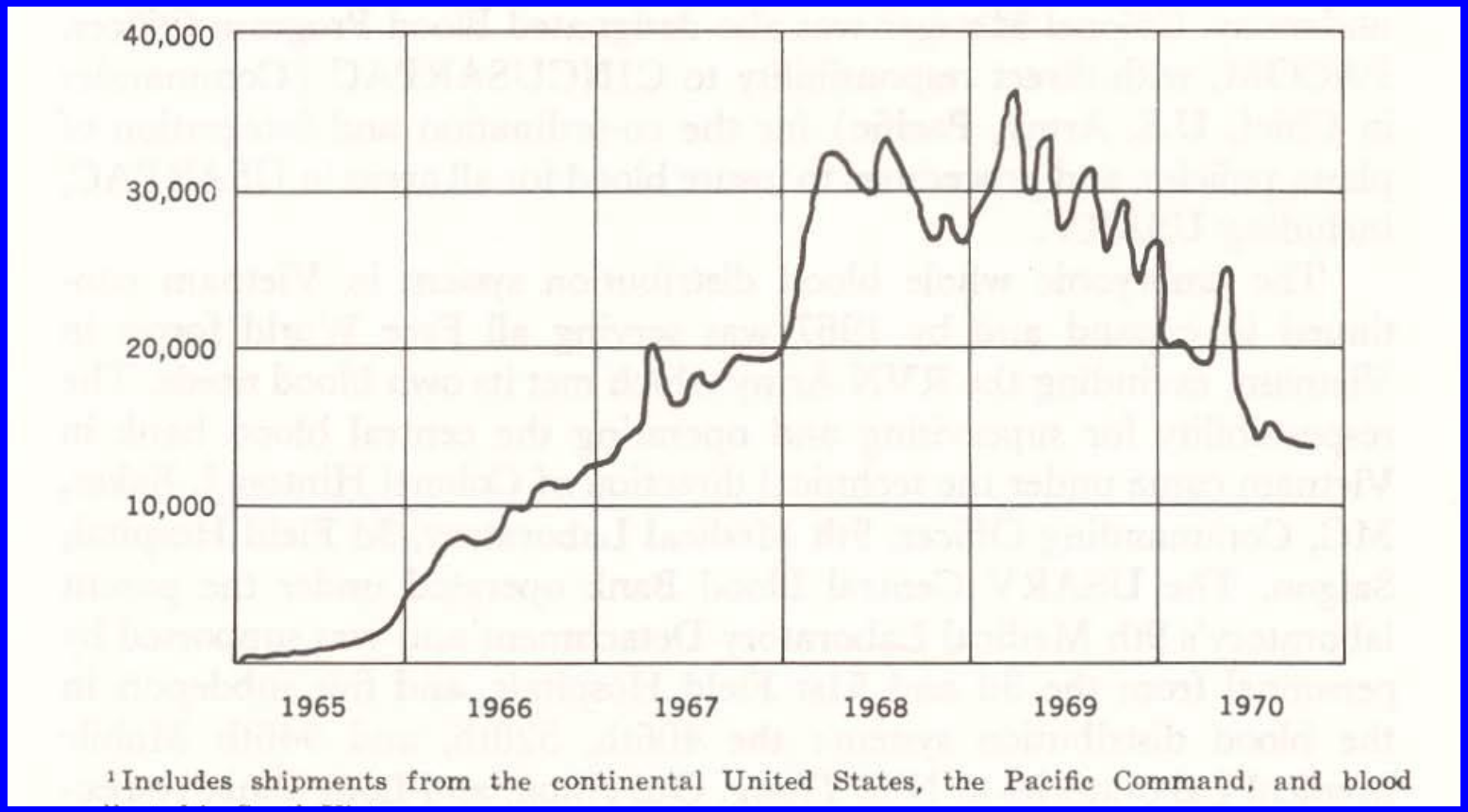
Whole blood advantage #1

Long history of transfusing WB

J-B Denis used lamb blood for transfusion in 1667



US Military use of low titer group O WB in Vietnam (also towards end of Korea)



1967-1969 = 364,900 WB transfused

US Policy – continue low titer O type whole blood if received more than 4u

Courtesy Col (Dr.) Alan Murdock

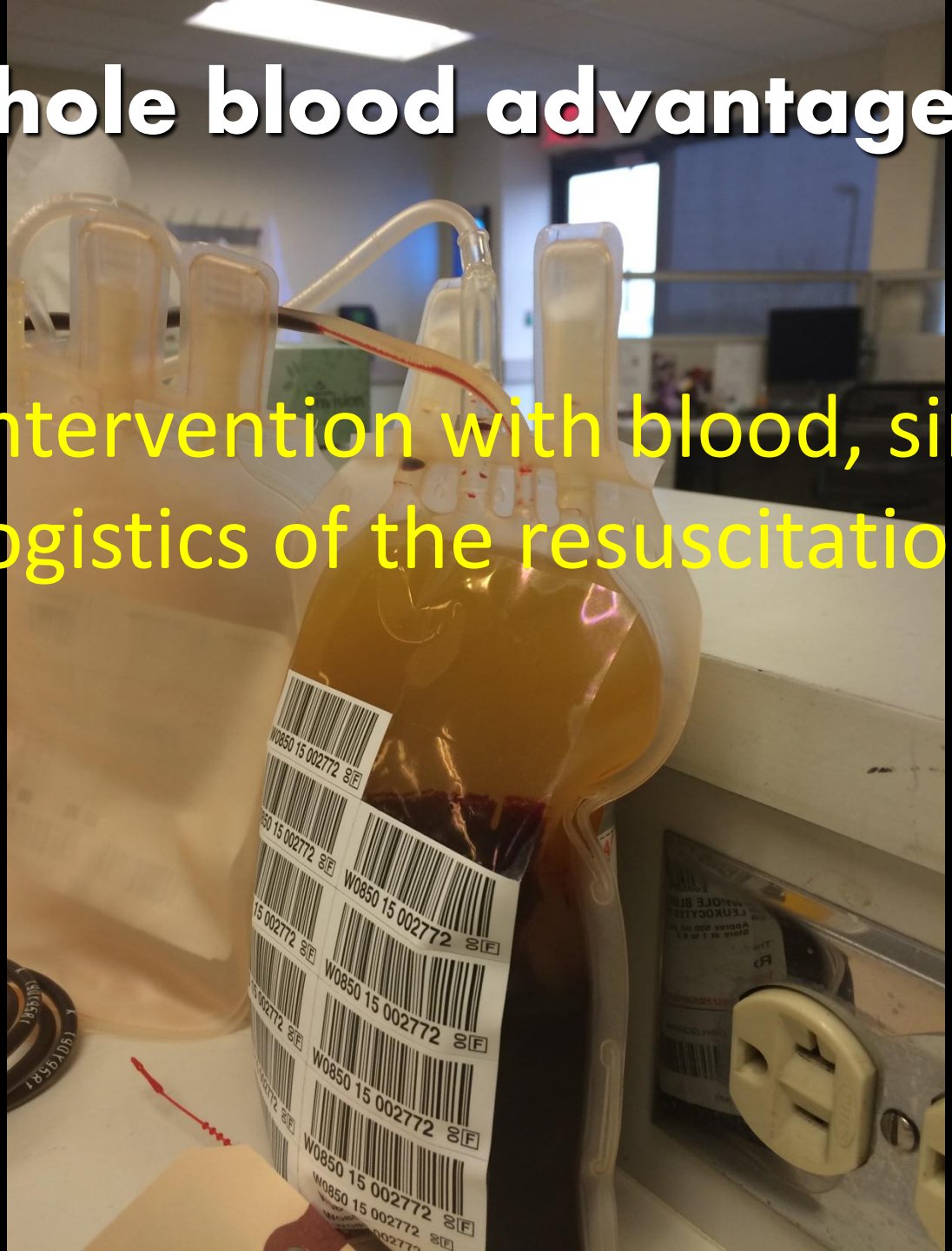
Israeli military transfused 894 units of untitered WB during Yom Kippur war, 1973

Berseus et al. *Transfusion* 2013:114S

Many modern armies are adopting LTOWB for resuscitating injured soldiers

Courtesy Dr. (COL) Miloš Bohoněk

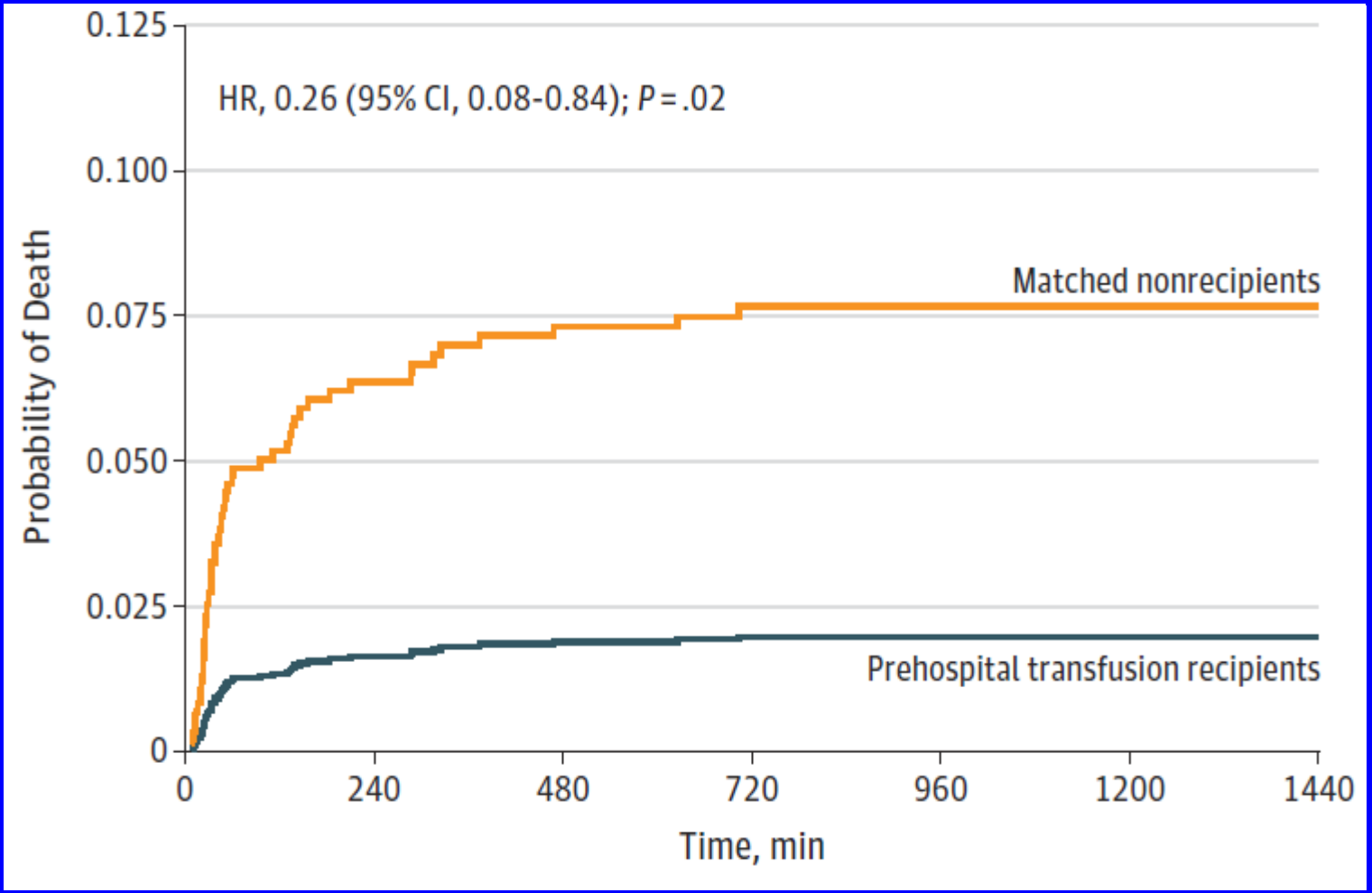
Whole blood advantage #2



Easier intervention with blood, simplifies logistics of the resuscitation

Early transfusion saves lives

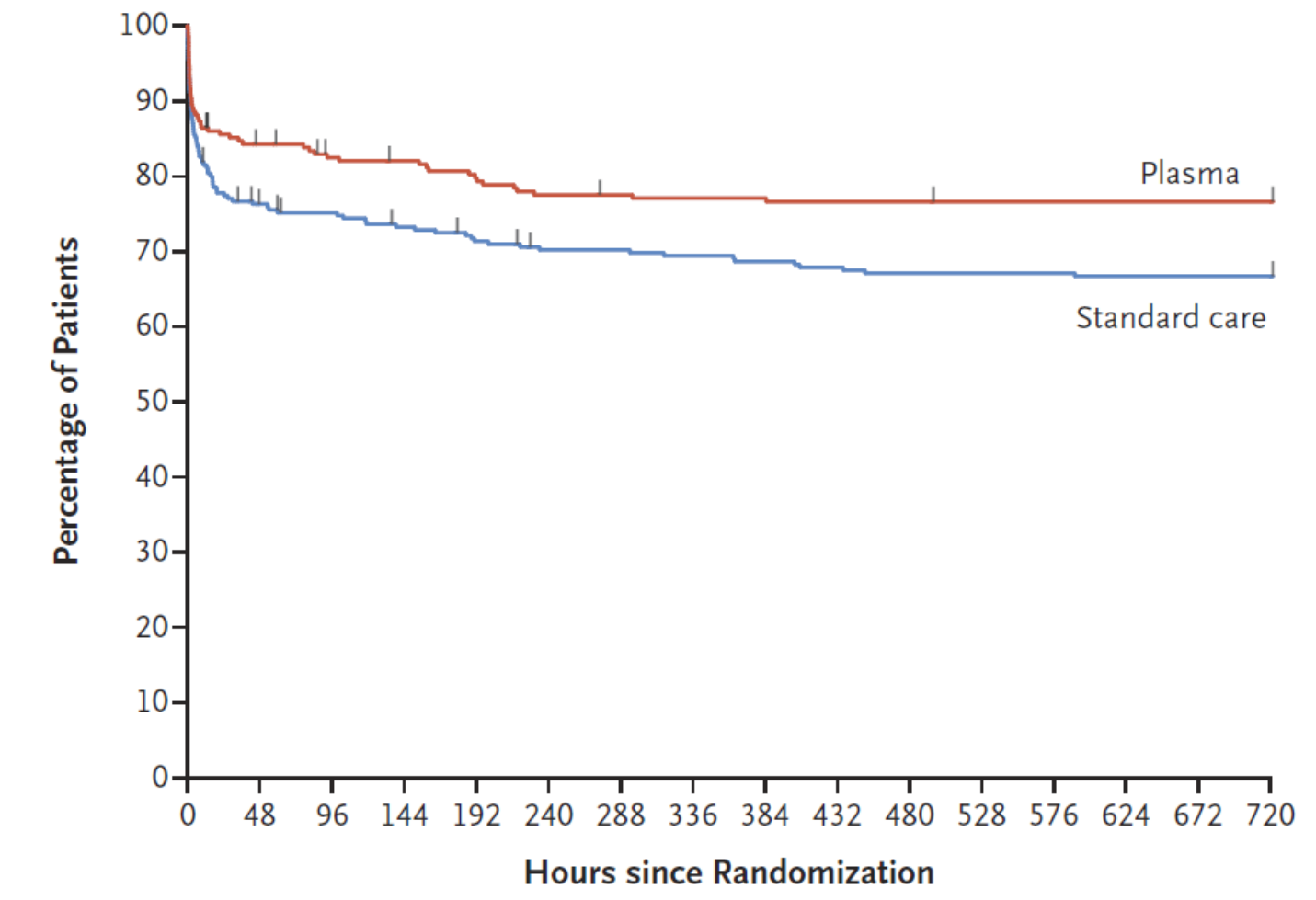
- Adjusted, retrospective US military data on 502 casualties
- 55 transfused pre-hospital with RBC only, plasma only, or RBC+plasma



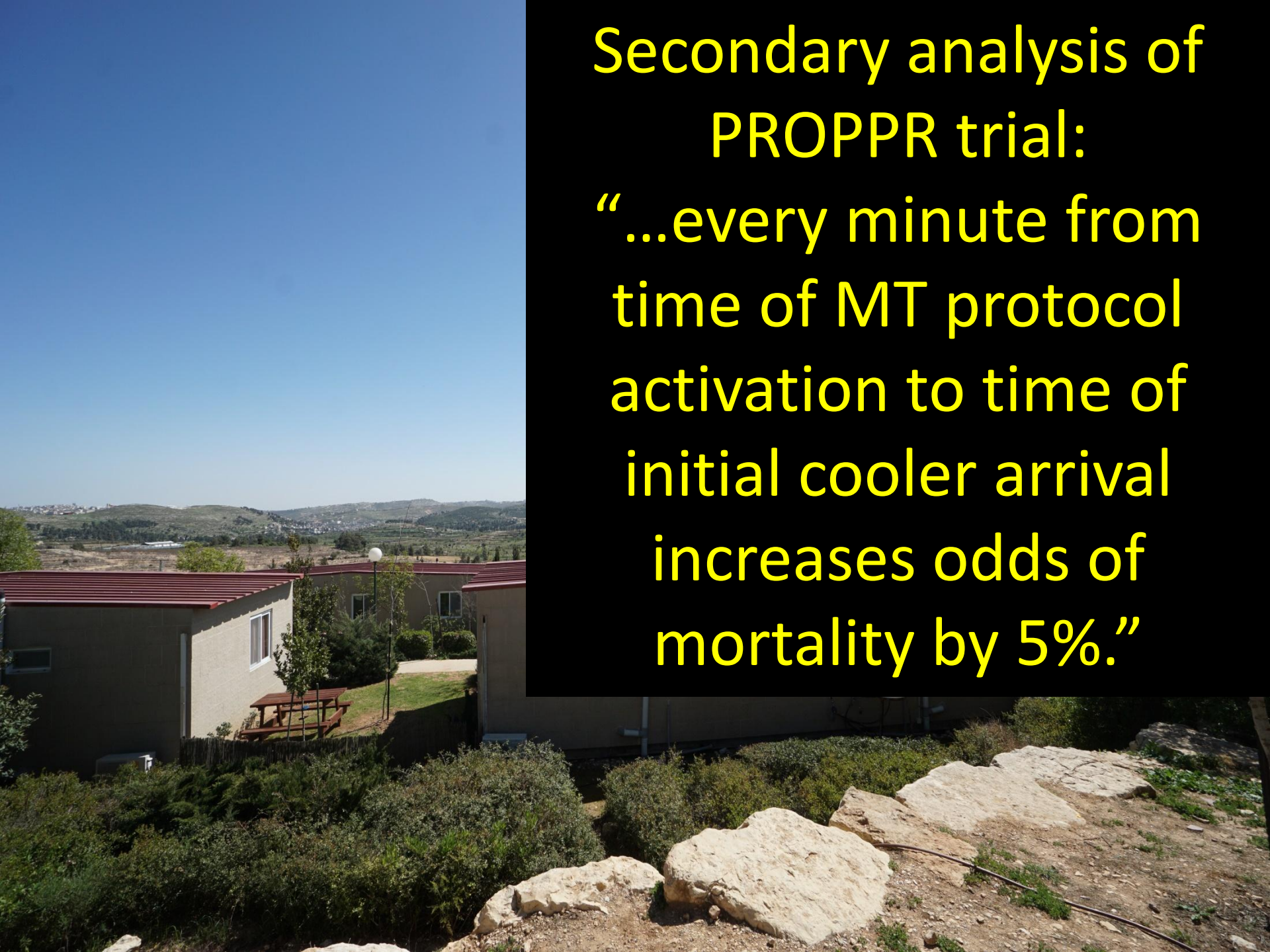
Shackelford SA et al. *JAMA* 2017;318:1581-1591

Early plasma transfusion saves lives

- Plasma improves mortality compared to S-of-C in aircraft-rescued trauma patients with *longer* transport times



Sperry JL et al. *NEJM* 2018;379:315-326



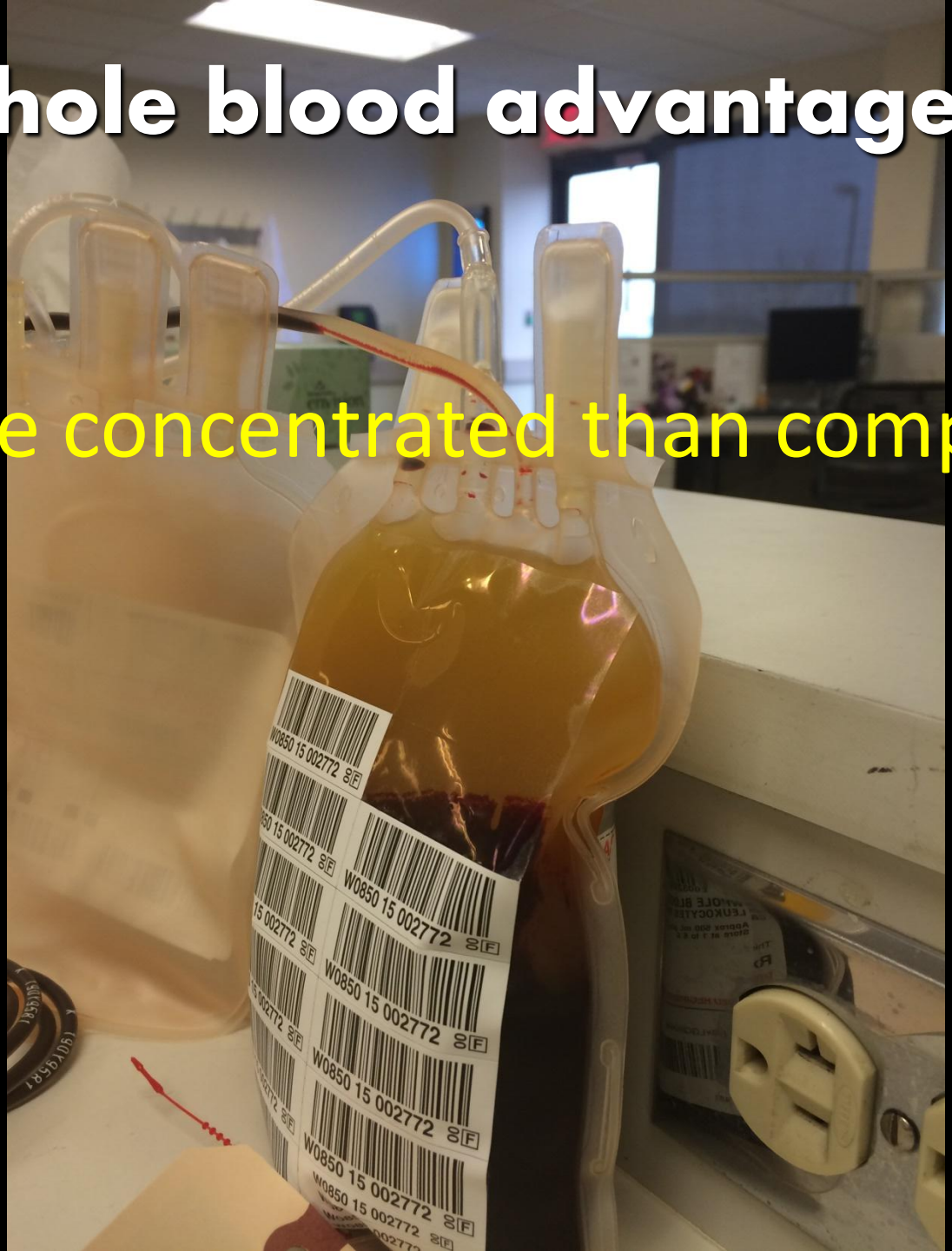
Secondary analysis of PROPPR trial:

"…every minute from time of MT protocol activation to time of initial cooler arrival increases odds of mortality by 5%."

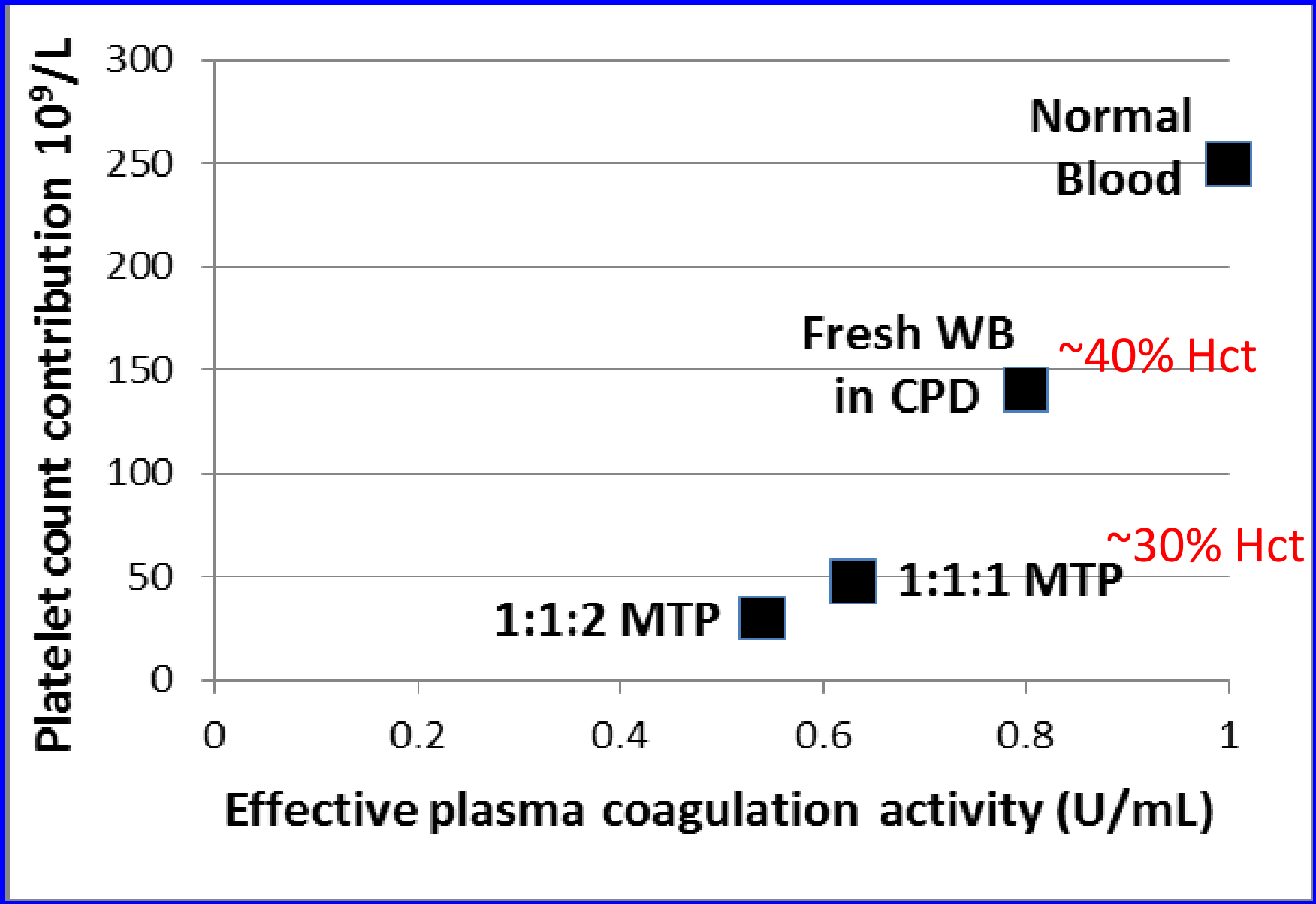
1 bag v. 3 – it makes a difference!

Whole blood advantage #3

It’s more concentrated than components



1:1:1 is not the same as WB



Courtesy Dr. John Hess

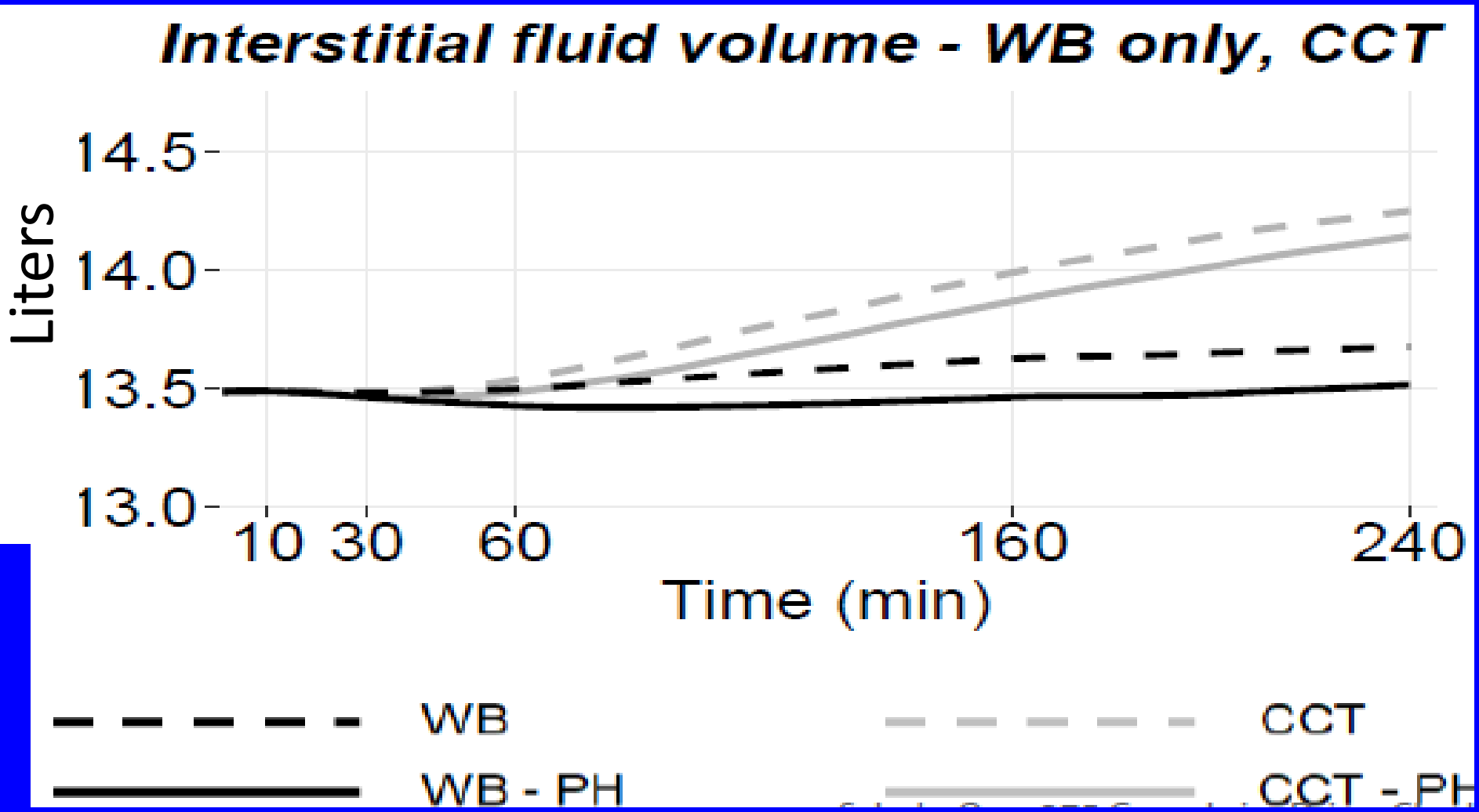
	Volume of CPD	Volume of AS	Total
Plasma	48	0	48
RBC	8	110	118
APLT	35	0	35
WB PLT	14	0	14
WB	70	0	70

A lot of extra fluid in reconstituted WB

Imagine a 10 unit massive transfusion

- 1:1:1 = 1800 mL of CPD/AS

Simulation of 20 unit massive transfusion



Seheult J et al. *Transfusion* in press

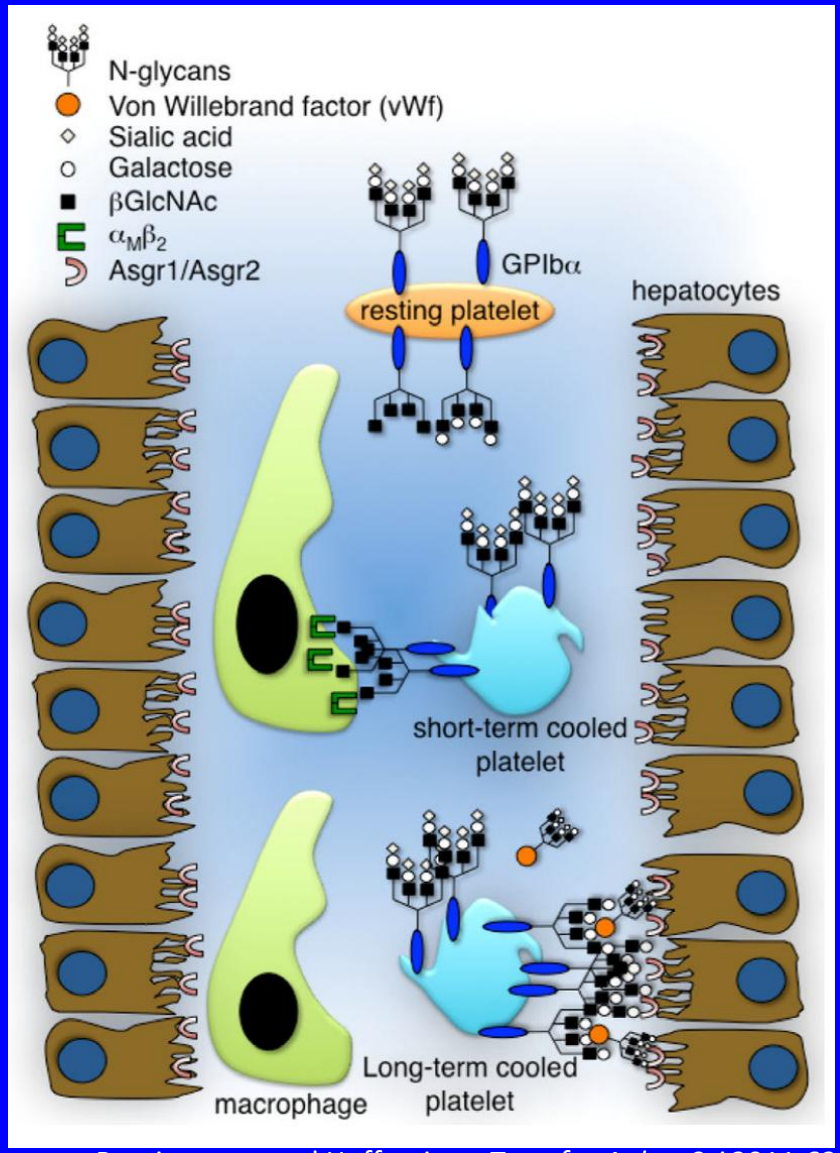
Whole blood advantage #4

Cold stored platelets might be great, again!

What's with cold storage of platelets?

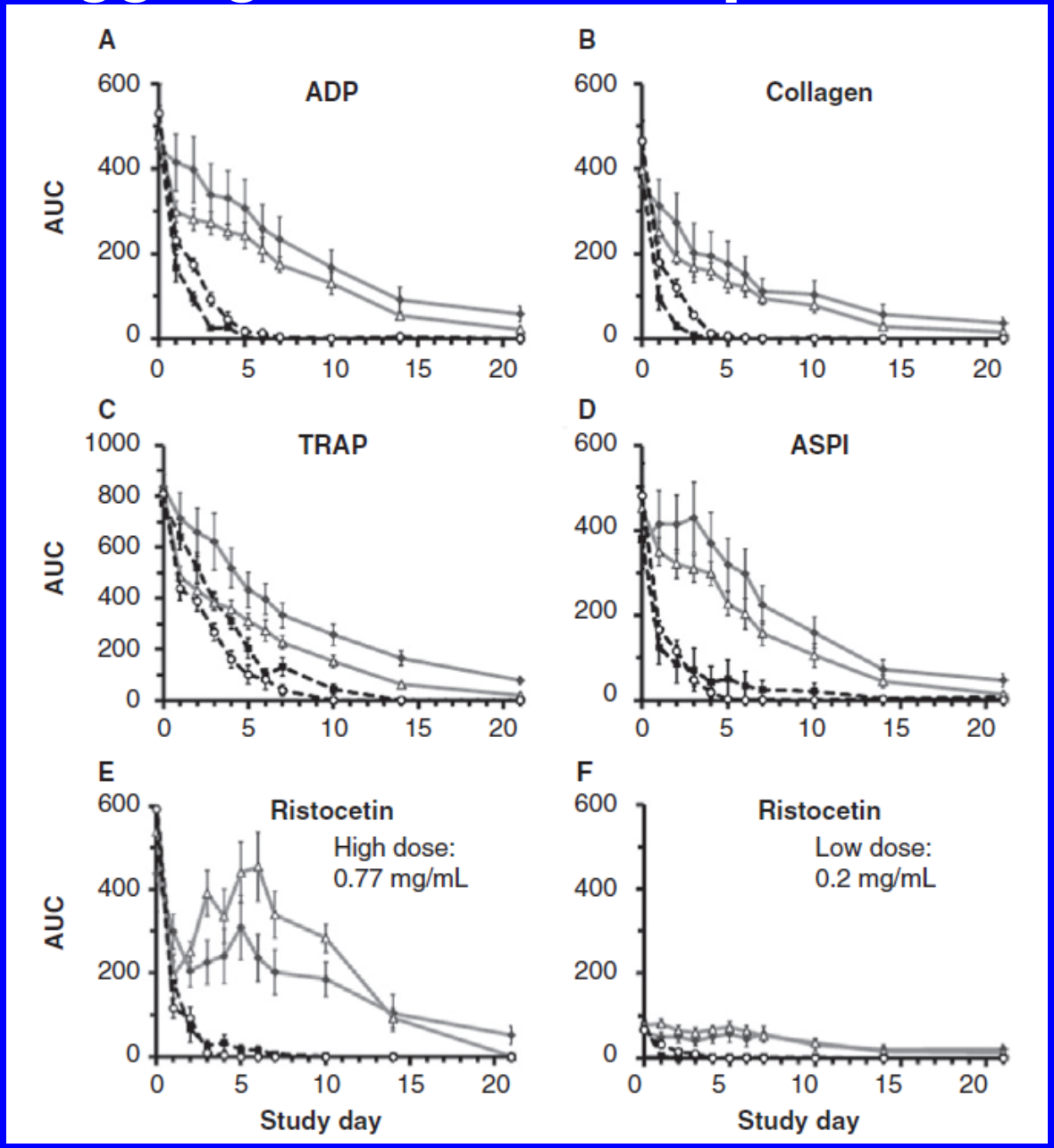
- This is how they were initially kept
- Reduces bacteria risk
- *In vivo* survival is shorter than RT PLTs
  - RT: 56% recovery, 161 hr survival
  - Cold: 23% recovery, 33 hr survival

Vostal et al. *Transfusion* 2018:25



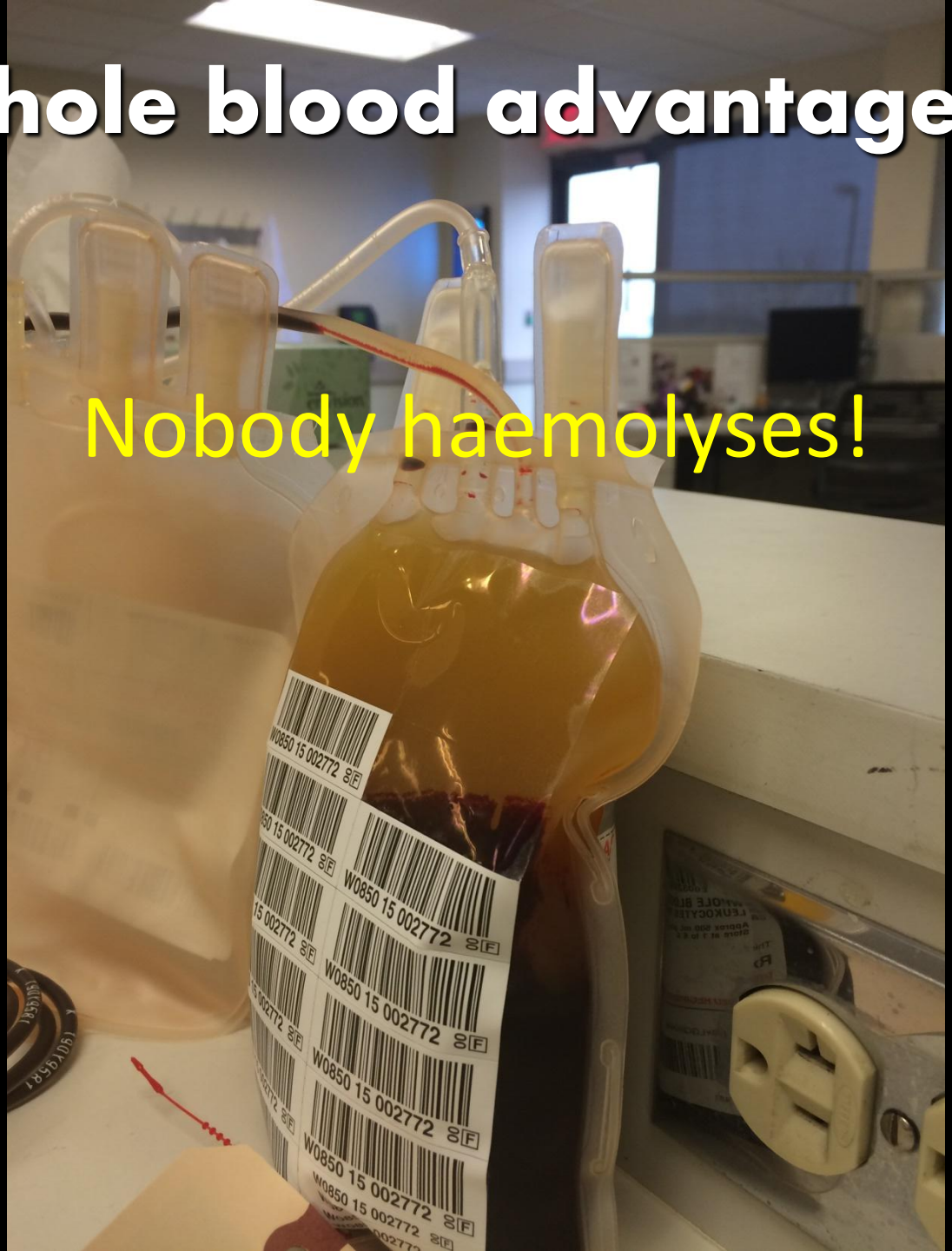
Rumjantseva and Hoffmeister *Transfus Apher Sci* 2011:63

PLT aggregation in WB improved at 4ºC



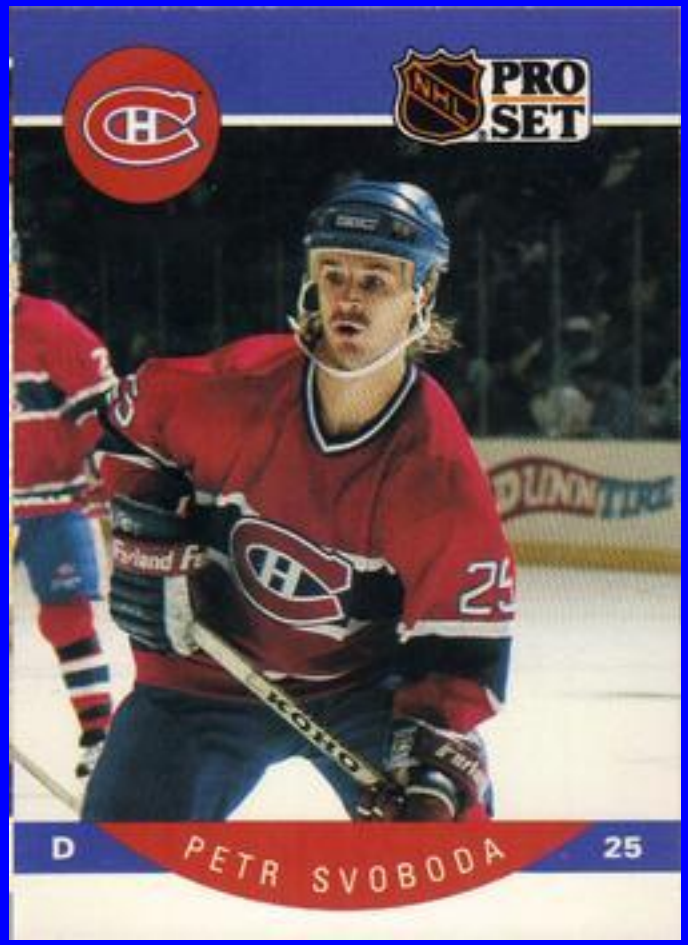
Pidcoke et al.*Transfusion* 53:173S

Whole blood advantage #5



The Pittsburgh approach to use of WB in *adult* trauma

- Started in December 2014
- Male trauma patients with hypotension of any age
  - Female trauma patients ≥50
- 6 WB units kept in the ED fridge *for immediate use*
  - At least 6 more kept in the blood bank
- After these 6 units administered, conventional products administered as per TEG results

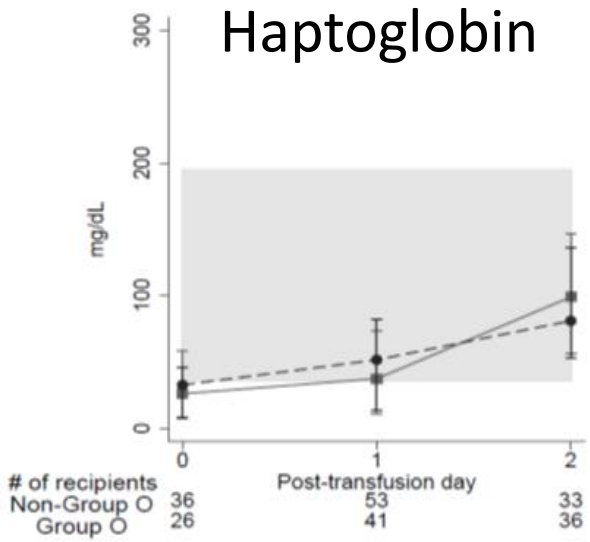


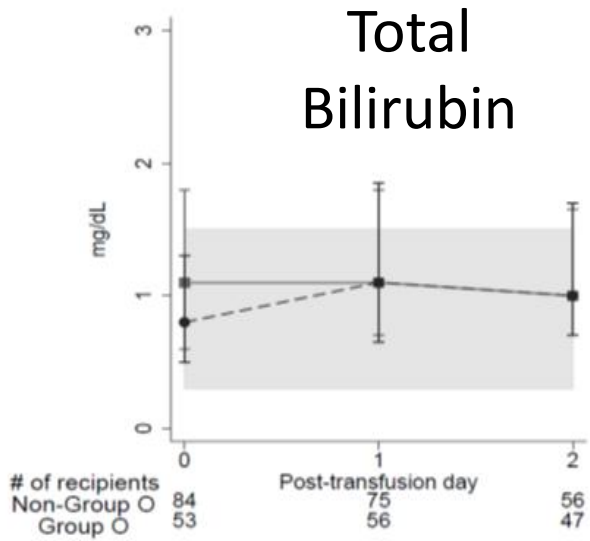
The Pittsburgh approach to use of WB in *adult* trauma

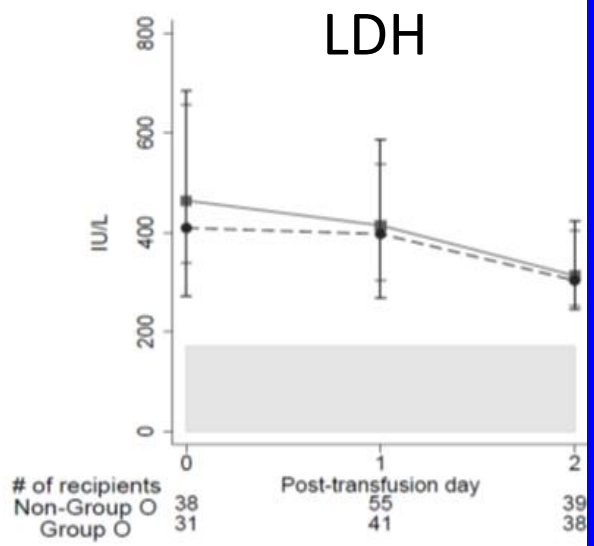
- Group O + WB units
  - Collected with PLT sparing inline leukoreduction filter
  - Titer of both anti-A and –B <50
  - Titers performed on every unit every time
  - Male only donors for TRALI risk mitigation
- Stored as WB for 14 days
  - After day 14 WB can be manufactured into an RBC unit up to day 21

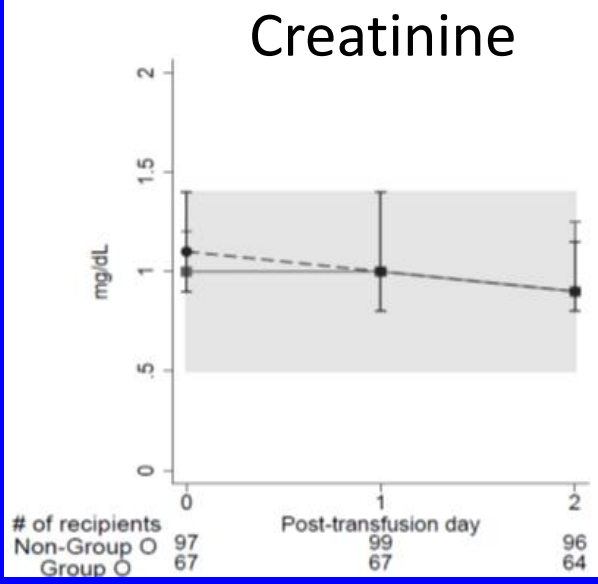
403 patients have received 829 LTOWB units

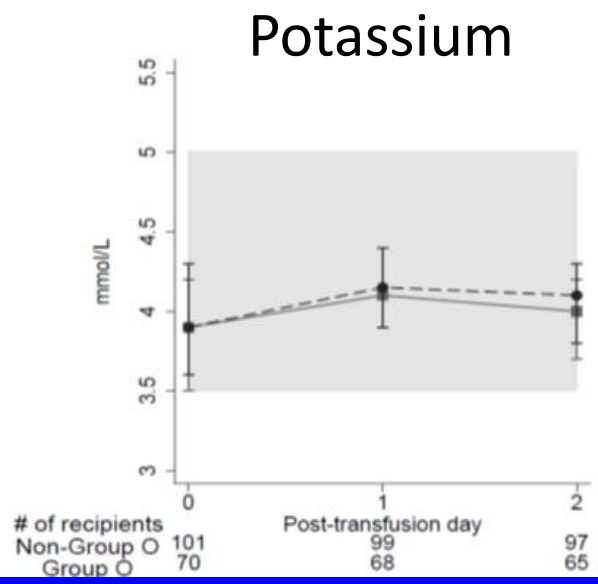
No haemolysis

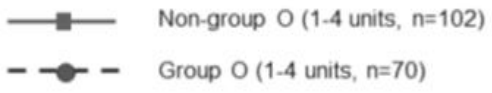






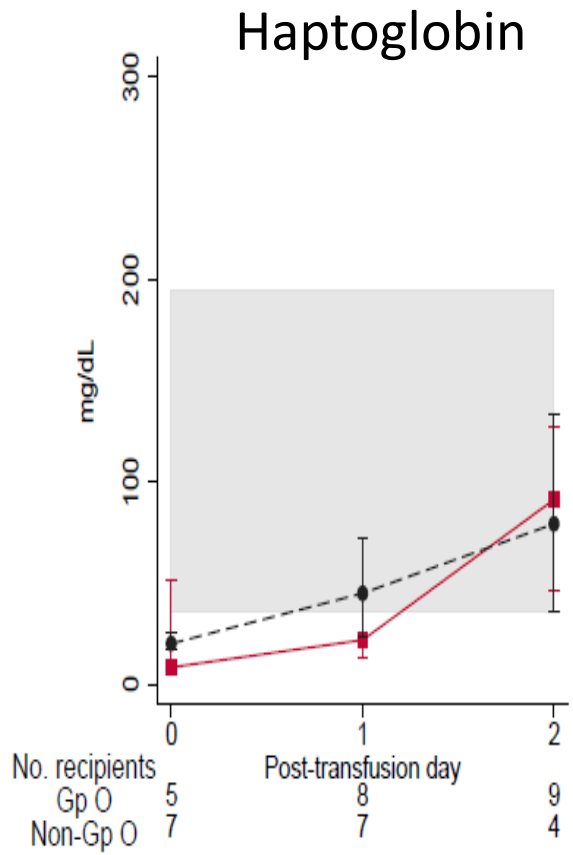


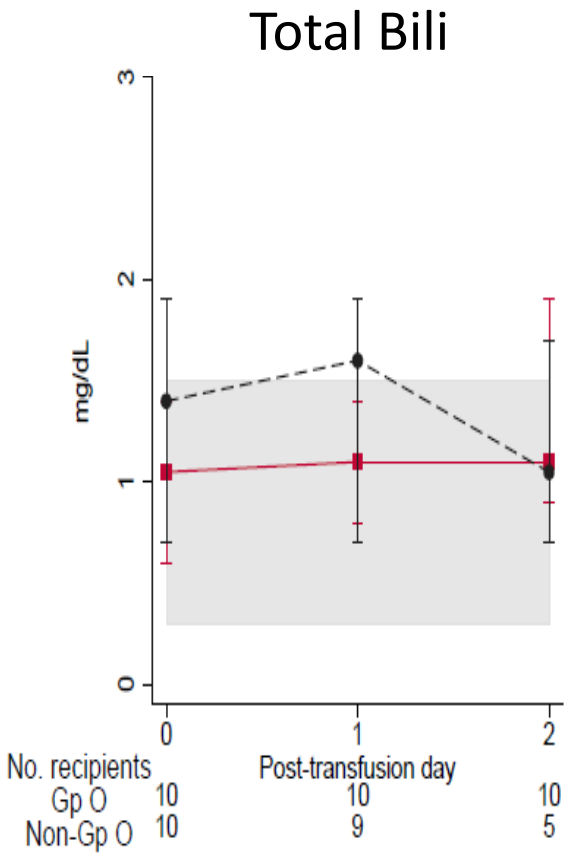


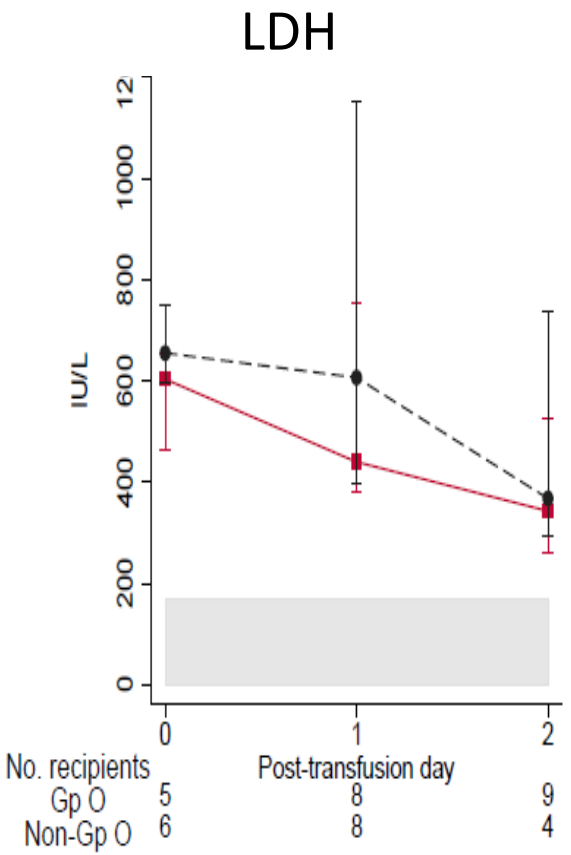


Seheult et al. *Transfusion* in press

No haemolysis amongst recipients of 3 and 4 WB units





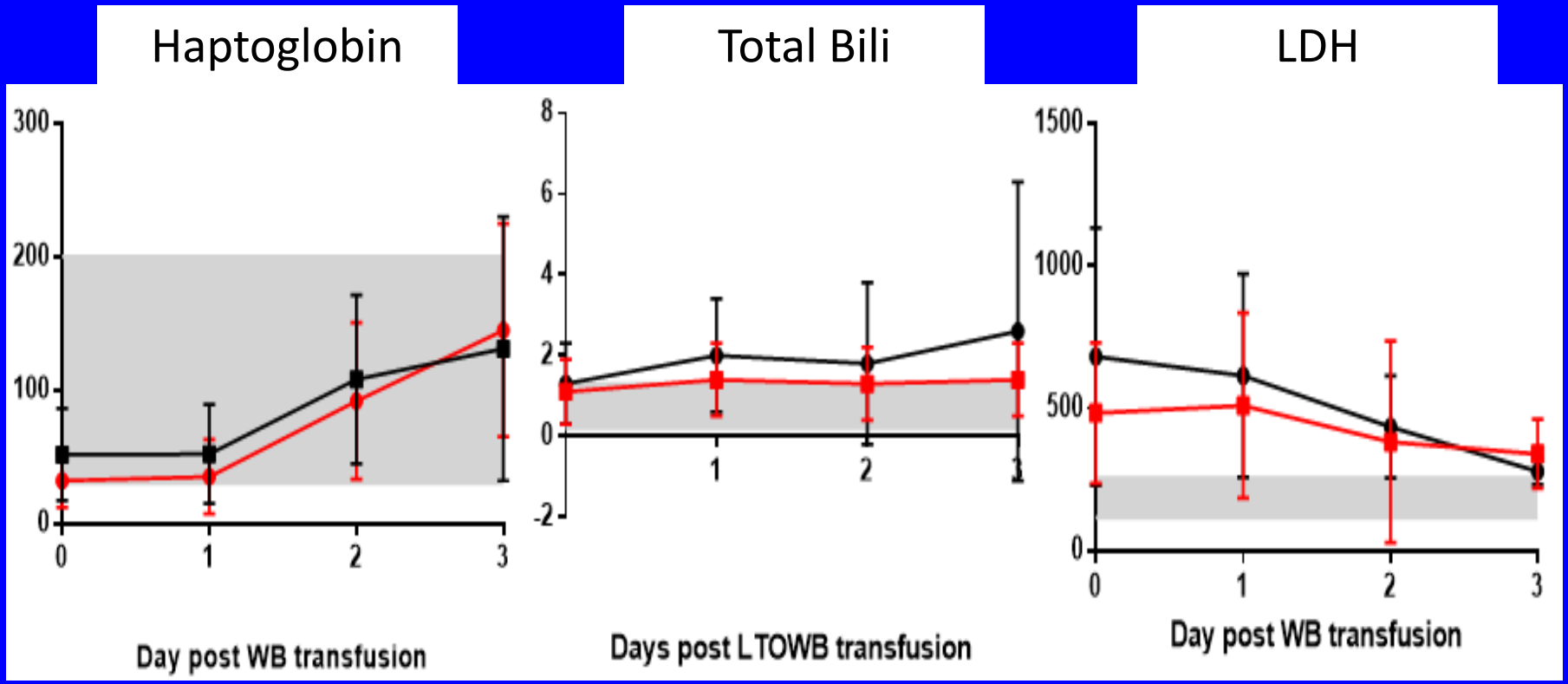


Non group O

Group O

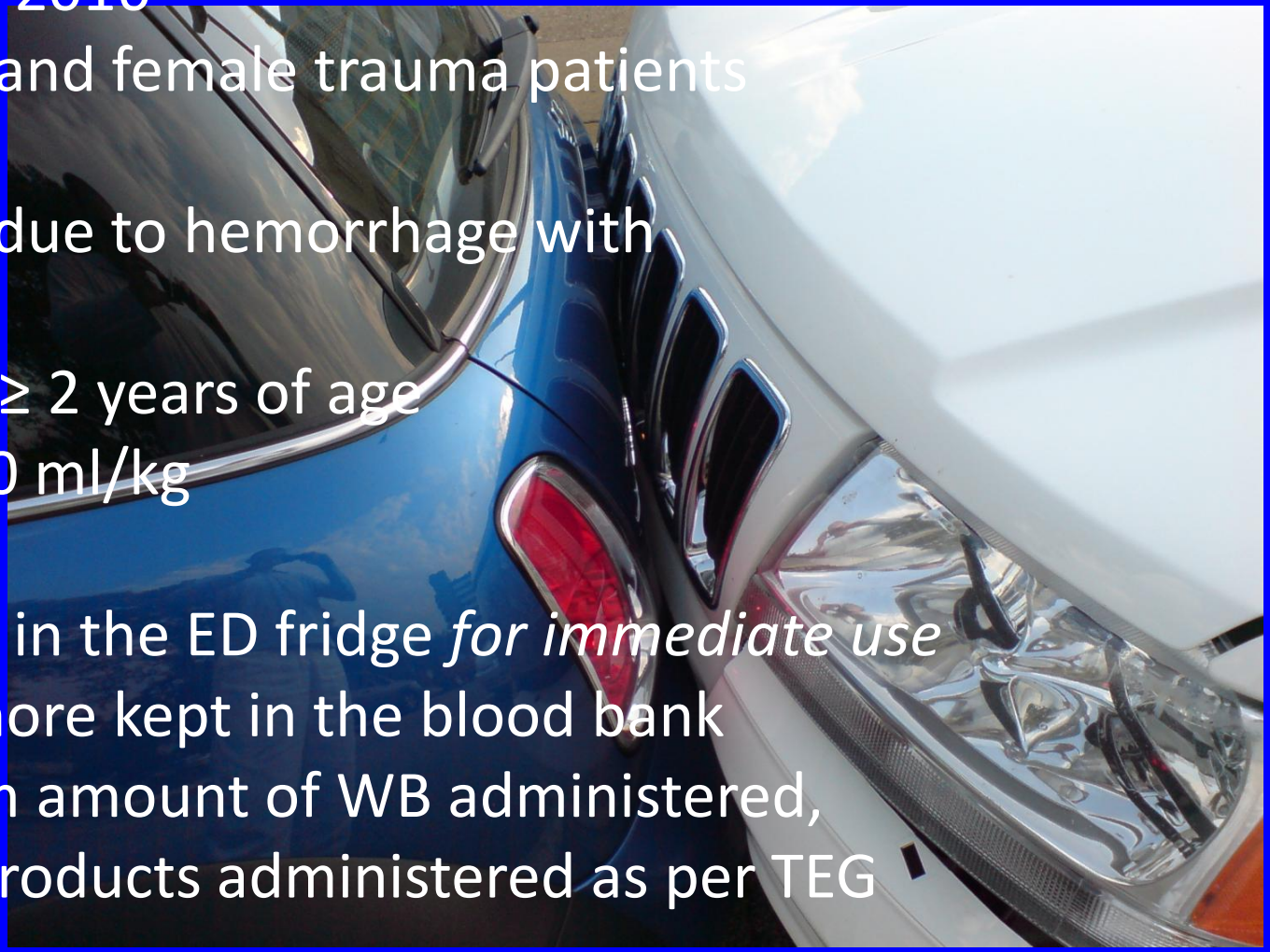
Seheult et al. *Transfusion* in press

No haemolysis amongst recipients of 4-6 WB units



The Pittsburgh approach to use of WB in *paeds* trauma

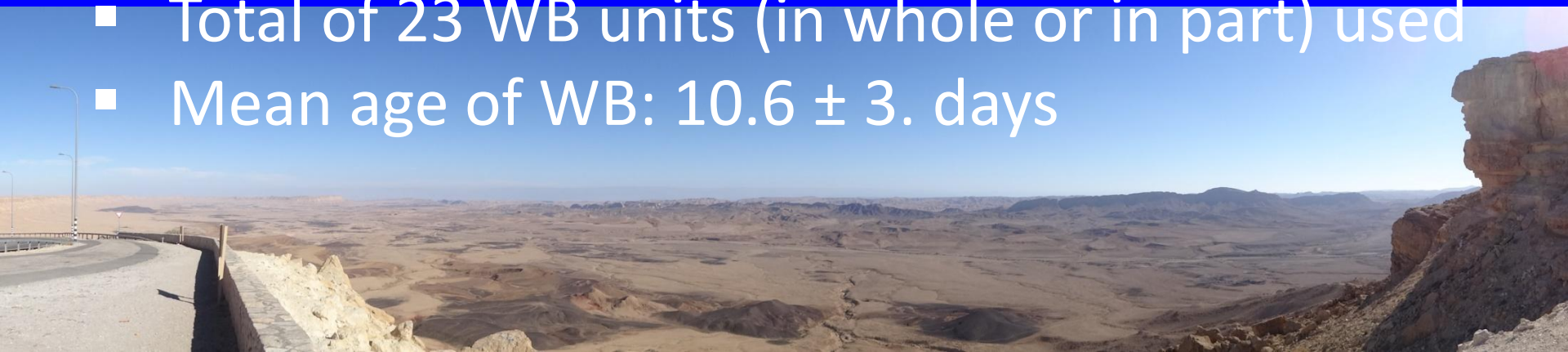
- Started in June 2016
- For ***both*** male and female trauma patients
- O neg WB
- Signs of shock due to hemorrhage with hypotension
- ≥ 10 kg and/or ≥ 2 years of age
- Maximum of 30 ml/kg



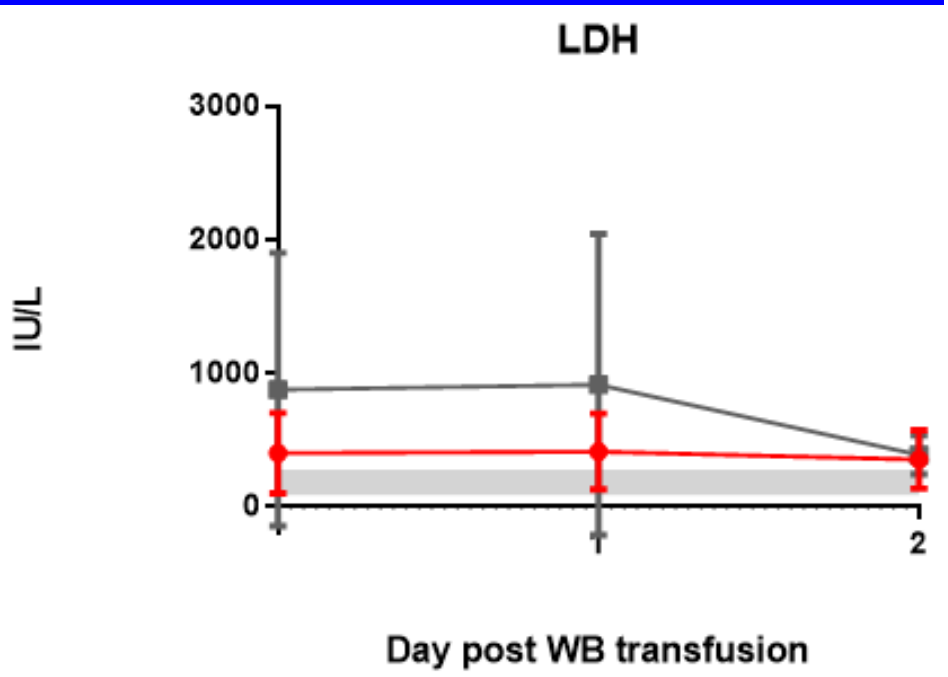
- 1 WB unit kept in the ED fridge *for immediate use*
  - At least 1 more kept in the blood bank
- After maximum amount of WB administered, conventional products administered as per TEG results

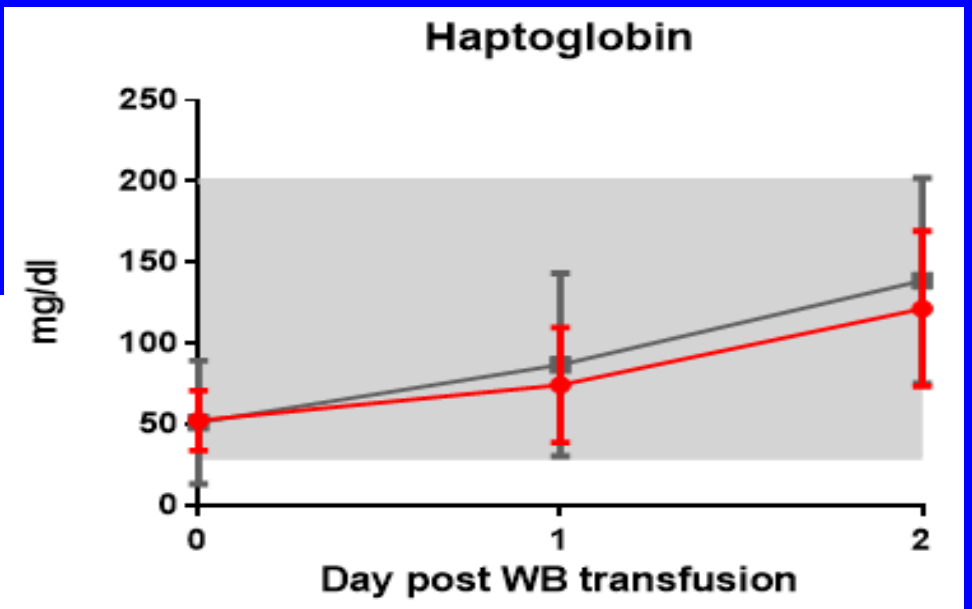
WB in paeds trauma!

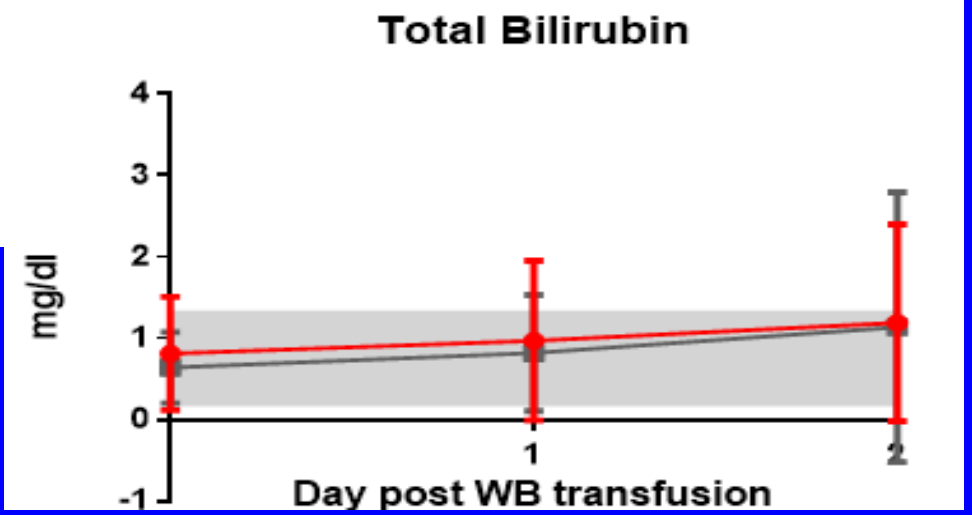
- 20 patients have received WB for trauma resuscitation
- Mean age 11.1 ± 4.9 years old
- 10 group O, 10 non-O (all A)
  - Two especially sick group O patients
  - 1 group O patient died shortly after LTOWB receipt
- 8 female, 12 male
- Mean # units per patient: 1.2 ± 0.4 units
  - Total of 23 WB units (in whole or in part) used
  - Mean age of WB: 10.6 ± 3. days



Haemolysis? No.



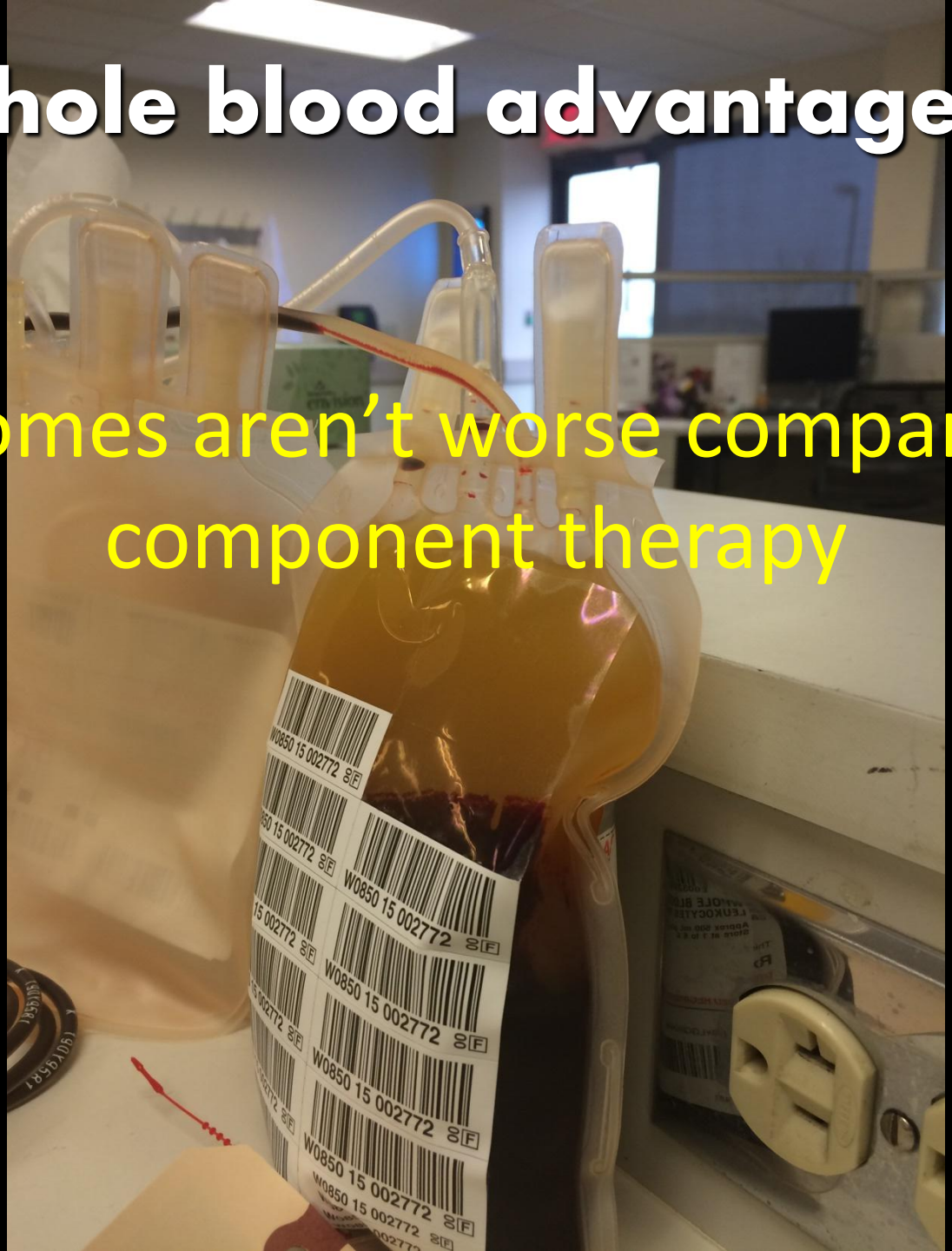




Non-group O

Group O

Whole blood advantage #6



Outcomes aren’t worse compared to component therapy

Seheult et al. *Transfusion* in press

	Component therapy (n=135)	LTOWB (n=135)	
In-hospital mortality, (%)	33/135 (24.4)	25/135 (18.5)	0.24
6-hour mortality, (%)	5/135 (3.7)	4/135 (3.0)	0.74
24-hour mortality, (%)	17/135 (12.6)	12/135 (8.9)	0.33
Death due to bleeding	6/135 (4.4)	8/135 (5.9)	0.58
Death due to traumatic head injury	20/135 (14.8)	11/135 (8.2)	0.09
Death due to multi-organ failure	7/135 (5.2)	6/135 (4.4)	0.78
Time to normalization of elevated plasma lactate levels, hours	13.2 (4.4 – 26.8)	8.1 (3.7 – 15.4)	0.05
Acute kidney injury, (%)			
Increased creatinine x 1.5 over baseline	8/126 (6.4)	10/126 (7.9)	0.63
Increased creatinine x 2 over baseline	0/126 (0)	2/126 (1.6)	0.16
Increased creatinine x 3 over baseline or absolute rise in creatinine≥0.5mg/dL or any post-admission creatinine ≥ 4.0 mg/dL	10/126 (7.9)	13/126 (10.3)	0.51
Hospital length of stay, days	13.0 (5.0 – 19.0)	12.0 (4.0 – 22.0)	0.60
ICU length of stay, days	4.0 (1.0 – 10.0)	3.0 (1.0 – 9.0)	0.16
ICU free days	6.0 (1.0 – 10.0)	5.0 (1.0 – 11.0)	0.32
Days on ventilator	1.0 (0 – 6.0)	1.0 (0 – 5.0)	1.00
Ventilator free days	9.0 (2.0 – 14.0)	8.0 (2.0 – 14.0)	0.45

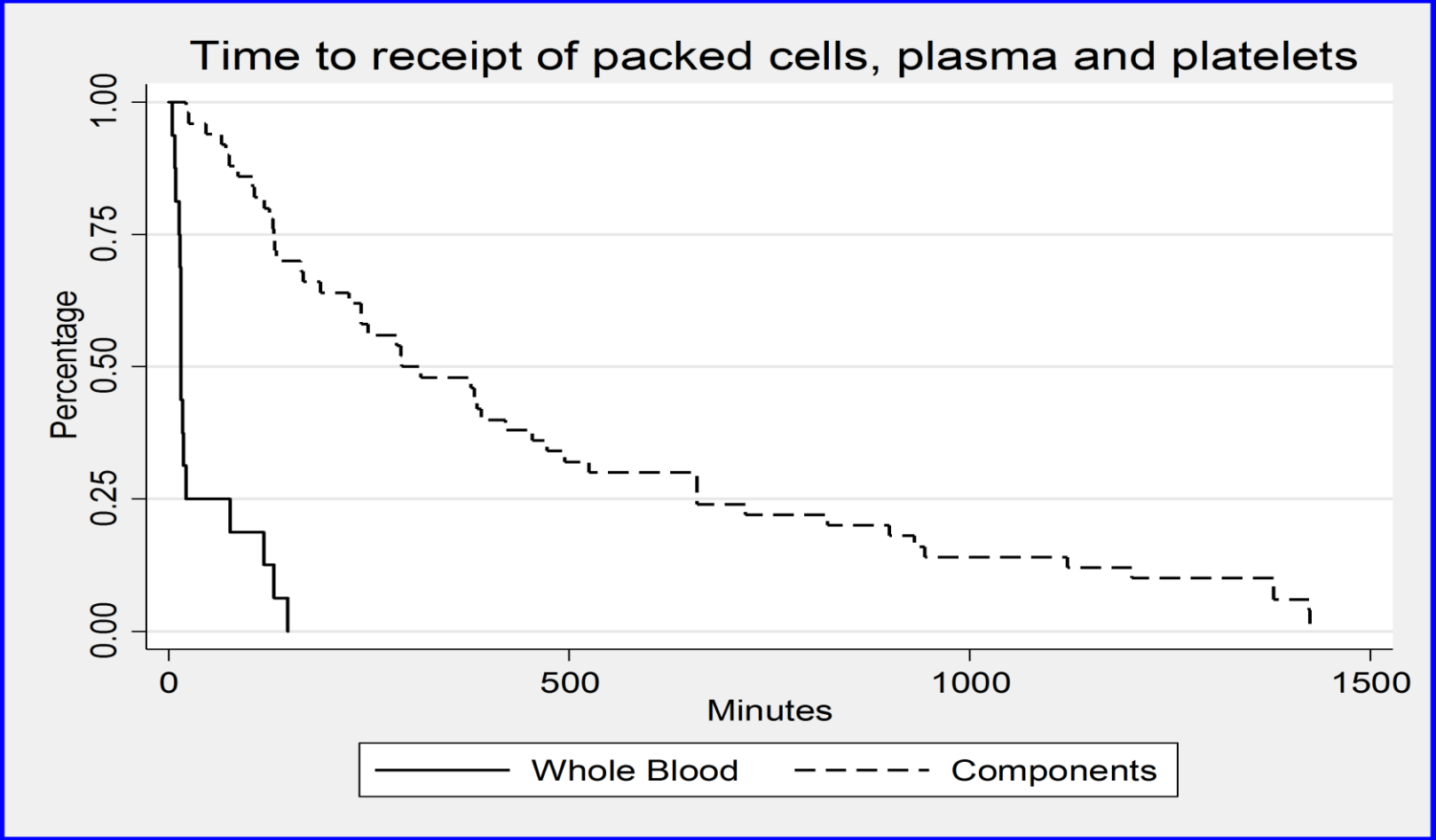
Do you like ratios?

- Mean Plasma:RBC ratio
  - LTOWB group : 1.00 (0.80-1.09)
  - Conventional components: 0.00 (0-1.00)
  - P<0.01

- Mean PLT:RBC ratio
  - LTOWB group: 1.00 (0.50-1.00)
  - Conventional components: 0 (0-0.67)
  - P<0.01

WB makes it easier to (initially) provide balanced resuscitation

- Time from ED admission until administration of WB (n=18) or at least 1 RBC, plasma, and PLT in historical cohort (n=50)



Leeper CM et al. JAMA Peds 2018 *in press*

Some outcomes in paeds trauma

- 18 WB recipients compared to 307 peds trauma patients who received at least 1 uncrossmatched RBC unit

	Whole Blood cohort n=18	Historical cohort n=307	p value
Mortality	44%	34%	0.20
Hospital Length of Stay (all patients)	7.5 (3-13)	9 (2-19)	0.48
ICU Length of Stay	3.5 (2-6)	4 (1-9)	0.71
Ventilator Days	2 (1-5)	2 (0-7)	0.75

Conclusions

- WB for use in civilian trauma is feasible
- It's safe
- Improving logistics of resuscitation is a **BIG** deal
- Efficacy remains to be definitively determined, but looking good!
- Probably the ideal pre-hospital resuscitation fluid
- Leukoreduction: personal preference


Fire away!
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